

CLAIMS

We claim:

1. An antibody that specifically binds to HIP1 but does not specifically bind
5 to the normal epithelium of prostate or colon.

2. The antibody of Claim 1, wherein said antibody binds to the cancerous
epithelium of colon or prostate but does not bind to the normal epithelium of prostate or
colon.

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3. The antibody of Claim 1, wherein said antibody is a monoclonal antibody.

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4. The monoclonal antibody of Claim 3, wherein said antibody has
substantially the same properties as antibodies secreted by a hybridoma selected from the
group consisting of those deposited as ATCC numbers pending.

5. The monoclonal antibody of Claim 4, wherein said antibody is secreted by
a hybridoma with ATCC deposit number pending.

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6. The monoclonal antibody of Claim 4, wherein said antibody is secreted by
a hybridoma with ATCC deposit number pending.

7. The monoclonal antibody of Claim 4, wherein said antibody specifically
binds to HIP1 protein with low background binding.

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8. The monoclonal antibody of Claim 4, wherein said antibody binds to
human and mouse HIP1.

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9. A method for detecting cancer, comprising:

- a) providing a sample from a subject suspected of having cancer; and
- b) detecting the presence or absence of HIP1 in said sample.

10. The method of Claim 9, wherein the presence of HIP1 in said sample is indicative of cancer in said subject.

5 11. The method of Claim 9, wherein said cancer is selected from the group consisting of prostate cancer and colon cancer.

12. The method of Claim 9, wherein said sample is a tumor sample.

10 13. The method of Claim 9, wherein said sample is a tissue sample.

14. The method of Claim 13, wherein said tissue sample is selected from the group consisting of prostate tissue and colon tissue.

15 15. The method of Claim 9, wherein said sample is selected from the group consisting of serum, plasma, blood, and urine.

16. The method of Claim 8, wherein said detecting HIP1 comprises detecting the presence of HIP1 mRNA.

20 17. The method of Claim 16, wherein said detecting the presence of HIP1 mRNA comprises exposing said HIP1 mRNA to a nucleic acid probe complementary to at least a portion of said HIP1 mRNA.

25 18. The method of Claim 17, wherein said detecting the presence of HIP1 mRNA comprises a detection assay selected from the group consisting of a Northern blot, in situ hybridization, reverse-transcriptase polymerase chain reaction, and microarray analysis.

30 19. The method of Claim 9, wherein said detecting the presence of HIP1 comprises detecting the presence of a HIP1 polypeptide.

20. The method of Claim 17, wherein said detecting the presence of a HIP1 polypeptide comprises exposing said HIP1 polypeptide to an antibody that specifically binds to HIP1 but does not specifically bind to the normal epithelium of prostate or colon
5 and detecting the binding of said antibody to said HIP1 polypeptide.

21. The method of Claim 20, wherein said antibody is a monoclonal antibody.

22. The method of Claim 21, wherein said monoclonal antibody has
10 substantially the same properties as monoclonal antibodies secreted by a hybridoma selected from the group consisting of those deposited as ATCC numbers pending.

23. The method of Claim 9, wherein said method further comprises step c)
providing a prognosis to said subject.
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24. A method for characterizing tissue in a subject, comprising:
a) providing a tissue sample from a subject, wherein said tissue is selected from the group consisting of colon and prostate tissue; and
b) detecting the presence or absence of HIP1 in said sample, thereby characterizing said tissue sample.
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25. The method of Claim 24, wherein said tissue is tumor tissue.

26. The method of Claim 24, wherein said tissue is biopsy tissue.
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27. The method of Claim 24, wherein said detecting HIP1 comprises detecting the presence of HIP1 mRNA.

28. The method of Claim 27, wherein said detecting the presence of HIP1
30 mRNA comprises exposing said HIP1 mRNA to a nucleic acid probe complementary to at least a portion of said HIP1 mRNA.

29. The method of Claim 28, wherein said detecting the presence of HIP1 mRNA comprises a detection assay selected from the group consisting of a Northern blot, in situ hybridization, reverse-transcriptase polymerase chain reaction, and microarray analysis.

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30. The method of Claim 24, wherein said detecting the presence of HIP1 comprises detecting the presence of a HIP1 polypeptide.

31. The method of Claim 30, wherein said detecting the presence of a HIP1 10 polypeptide comprises exposing said HIP1 polypeptide to an antibody that specifically binds to HIP1 but does not specifically bind to the normal epithelium of prostate or colon and detecting the binding of said antibody to said HIP1 polypeptide.

32. The method of Claim 31, wherein said antibody is a monoclonal antibody.

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33. The method of Claim 32, wherein said monoclonal antibody has substantially the same properties as monoclonal antibodies secreted by a hybridoma selected from the group consisting of those deposited as ATCC numbers pending.

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34. The method of Claim 24, wherein said tissue sample is a post-surgical prostate tumor tissue sample and said method further comprises the step of c) identifying a risk of prostate specific antigen failure based on said detecting the presence of HIP1.

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35. The method of Claim 24, wherein said tissue sample is prostate tumor tissue and said characterizing comprises identifying a stage of prostate cancer in said prostate tumor tissue.

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36. The method of Claim 35, wherein said stage is selected from the group consisting of high-grade prostatic intraepithelial neoplasia, benign prostatic hyperplasia, prostate carcinoma, and metastatic prostate carcinoma.

37. The method of Claim 24, wherein said tissue sample is prostate tumor tissue and said method further comprises the step of c) identifying the risk of said tumor metastasizing based on said detecting the presence of HIP1.

5 38 The method of Claim 24, wherein said tissue sample is post-surgical prostate tumor tissue and said method further comprises the step of c) identifying the risk of said tumor recurring based on said detecting the presence of HIP1.

10 39. A kit for characterizing cancer in a subject, comprising:

- a) a reagent that specifically detects the presence or absence of expression of HIP1; and
- b) instructions for using said kit for characterizing cancer in said subject.

15 40. The kit of Claim 39, wherein said reagent comprises an antibody that specifically binds to HIP1 but does not specifically bind to the normal epithelium of prostate or colon.

20 41. The kit of Claim 40, wherein said antibody is a monoclonal antibody.

42. The kit of Claim 41, wherein said monoclonal antibody has substantially the same properties as monoclonal antibodies secreted by a hybridoma selected from the group consisting of those deposited as ATCC numbers pending.

25 43. The kit of Claim 39, wherein said reagent comprises a nucleic acid probe that specifically binds to a HIP1 mRNA.

30 44. The kit of Claim 39, wherein said instructions comprise instructions required by the United States Food and Drug Administration for use in *in vitro* diagnostic products.

45. A method of screening compounds, comprising:

- a) providing
 - i) an cell sample comprising cancerous epithelial cells; and
 - ii) one or more test compounds; and
- 5 b) contacting said sample with said test compound; and
- c) detecting a change in HIP1 expression in said sample in the presence of said test compound relative to the absence of said test compound.

46. The method of Claim 45, wherein said contacting said sample with said
10 test compound results in death of said cancerous epithelial cells.

47. The method of Claim 45, wherein said contacting said sample with said test compound results in impaired proliferation of said cancerous epithelial cells.

15 48. The method of Claim 45, wherein said epithelial cell sample is selected from the group consisting of prostate cancer cells and colon cancer cells.

49. The method of Claim 45, wherein said detecting comprises detecting HIP1 mRNA.

20 50. The method of Claim 45, wherein said detecting comprises detecting HIP1 polypeptide.

51. The method of Claim 45, wherein said cell is *in vitro*.

25 52. The method of Claim 45, wherein said cell is *in vivo*.

53. The method of Claim 45, wherein said test compound comprises an antisense compound.

30 54. The method of Claim 45, wherein said test compound comprises a drug.

55. The method of Claim 54, wherein said drug is an antibody.

56. The method of Claim 54, wherein said drug specifically binds to HIP1.

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57. A method of screening compounds, comprising:

a) providing

10 i) a first cell sample comprising cells expressing wild-type HIP1;

 ii) a second cell sample comprising cells, wherein said cells do not express HIP1;

 iii) one or more test compounds; and

b) contacting said first and seconds samples with said test compound;

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c) detecting a decrease in viability in said first sample relative to said second sample.

58. The method of Claim 57, wherein said decrease in viability is due to programmed cell death.

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59. The method of Claim 57, wherein said first and second cell samples comprise embryonic fibroblast cells.

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60. The method of Claim 58, wherein first cell sample comprises embryonic fibroblast cells derived from wild-type mice.

61. The method of Claim 59, wherein said second cell sample comprises embryonic fibroblast cells derived from HIP1 knockout mice.

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62. The method of Claim 57, wherein said first and second cell samples comprise first and second human cancer cell lines.

63. The method of Claim 62, wherein said second human cancer cell line is colo205 cells.

5 64. The method of Claim 57, wherein said test compound comprises a library of test compounds.

65. The method of Claim 57, wherein said test compound comprises a lipid analogue.

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66. The method of Claim 57, wherein said test compound binds to HIP1.

67. The method of Claim 66, wherein said test compound binds to the ENTH domain of HIP1.

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68. A composition comprising a mutant HIP1 nucleic acid sequence, said sequence lacking the ENTH domain.

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69. The composition of Claim 68, wherein said nucleic acid sequence comprises SEQ ID NO: 3.

70. A composition comprising a polypeptide encoded by the nucleic acid sequence of Claim 68.

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71. A composition comprising a mutant HIP1 polypeptide, wherein said polypeptide induces cell death when expressed in a cell.

72. The composition of Claim 71, wherein said mutant HIP1 polypeptide is lacking a ENTH domain.

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73. The composition of Claim 72, wherein said HIP1 polypeptide comprises SEQ ID NO: 4.

74. A nucleic acid sequence encoding the polypeptide of Claim 71.

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75. A non-human transgenic animal lacking a functional HIP1 gene.

76. The non-human transgenic animal of Claim 75, wherein said animal is a mouse.

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77. The non-human transgenic animal of Claim 75, wherein said animal comprises a knock-out of the HIP1 gene.

78. The non-human transgenic animal of Claim 76, wherein said knock-out of 15 the HIP1 gene is a conditional knock-out.

79. The non-human transgenic animal of Claim 75, wherein said animal comprises a knock-in of the HIP1 gene.

20 80. A composition comprising a drug, wherein said drug binds to wild type HIP1 but not a HIP1 ENTH deletion mutant, and wherein said drug inhibits HIP1 biological activity.

25 81. The composition of Claim 80, wherein said drug binds to the ENTH domain of HIP1.

82. The composition of Claim 81, wherein said drug is a lipid analogue.

30 83. The composition of Claim 82, wherein said lipid analogue is a phosphoinositide mimetic.